UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

March 2, 2015

MEMORANDUM

Subject: Acute Toxicity Review for EPA Reg. No. 6836-GTE
DP Barcode: D423566

From: Chris Jiang, Chemist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

Chris Jiang 3/2/15

Through: for Karen Hicks, Team Leader
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

To: Velma Noble PM 31/John C. Cowden
Regulatory Management Branch I
Antimicrobials Division (7510P)

Applicant: Lonza Inc.

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Poly(hexamethylenebiguanide) hydrochloride (PHMB)	0.0890
Octyl decyl dimethyl ammonium chloride	0.1333
Dioctyl dimethyl ammonium chloride	0.0534
Didecyl dimethyl ammonium chloride	0.0799
Alkyl (C_{14}, 50%; C_{12}, 40%; C_{16}, 10%) dimethyl benzyl ammonium chloride	0.1778
Other Ingredients	99.4666
Total	100.0000

BACKGROUND: The registrant has submitted an acute toxicity package for the registration of this wipe. The package includes a label, Confidential Statements of Formula for the basic formulation and alternate formulation 1, a compilation of acute toxicity studies (MRID 49445604), and waiver requests for acute inhalation toxicity and dermal sensitization.

RECOMMENDATIONS:

1. The test material was DS 6421 express liquid, undiluted.

2. The MRID 49445604 is a compilation of acute toxicity studies.

3. The acute inhalation is waived because of the low vapor pressure of all the components, low concentration of each component, and the fact that the product is a wipe.

4. The dermal sensitization is **not waived**. The active and inert ingredients may not be sensitizers, but the Agency is concerned about what happens when the components are mixed. The registrant will either conduct the study or cite some other product.

5. The acute toxicity profile for 6836-GTE is currently:

Study	MRID Number	Toxicity Category	Study Status
Acute Oral Toxicity	49445604	IV	Acceptable
Acute Dermal Toxicity	49445604	IV	Acceptable
Acute Inhalation Toxicity	49445604	IV	Waived
Primary Eye Irritation	49445604	II	Acceptable
Primary Skin Irritation	49445604	I	Acceptable
Skin Sensitization	49445604	?	Unacceptable

The policy on antimicrobial towelettes and wipes is under consideration by the Antimicrobial Division. Once the policy has been finalized, registrants will be informed if there are changes that need to be made regarding the registration process and if there are any additional data that must be submitted to the Division for review.

LABELING

No labeling can be prescribed at the present time.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (81-1, 870.1100)

Product Manager: Velma Noble
MRID No.: 49445604
Reviewer: Chris Jiang
Study Completion Date: Jan. 23, 2014
Study No.: MB 13-22158.01
Testing Laboratory: MB Research Laboratories
Author: Blair Yasso

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: DS 6421 Express Liquid, lot 5966-076B, clear colorless liquid
Dosage: 5000 mg/kg

Species: Female Sprague Dawley rats
Age: Twelve weeks
Pretest Weight: 206 to 221 grams
Source: Charles River, Raleigh, NC

Conclusions:

1. **LD_{50} (mg/kg):** $LD_{50} > 5000$ mg/kg
2. **The estimated LD_{50} is greater than 5000 mg/kg.**
3. **Toxicity Category**: IV **Classification**: Acceptable

Procedure (Deviations from 81-1): The Up-and-Down Procedure was used. Only female rats were used because females are typically more sensitive than males. These deviations had no impact on the integrity of the study.

Results:

Reported Mortality

Animal No.	Dose Level (mg/kg)	Short-Term Outcome	Long-Term Outcome
1	5000	O	O
2	5000	O	O
3	5000	O	X
4	5000	O	O

O = lived, **X** = died

Observations:
5000 mg/kg: Animal was active and healthy through the study except for mouse 3 who had dyspnea, piloerection, labored breathing, lethargy, hunched posture, unkempt appearance, chromorhinorhea, was emaciated, had few feces, had bloated abdomen, and had anogenital staining.

Gross Necropsy Findings:
5000 mg/kg: Gross necropsies were unremarkable except for mouse 3 who had a soiled anogetital area and intestines distended with gas.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (81-2, 870.1200)

Product Manager: Velma Noble
MRID No.: 49445604

Reviewer: Chris Jiang
Study Completion Date: Jan. 23, 2014
Study No.: MB 13-22158.02

Testing Laboratory: MB Research Laboratories
Author: Blair Yasso

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: DS 6421 Express Liquid, lot 5966-076B, clear colorless liquid
Dosage: 5000 mg/kg

Species: Five male and five female New Zealand White rabbits
Age: Thirty-two weeks
Pretest Weight: ♂: 2.8 to 3.2 kilograms; ♀: 3.1 to 3.4 kilograms
Source: Covance Research Products, Inc., Denver, PA

Conclusions:

1. **LD_{50} (mg/kg):** Males: LD_{50} > 5000 mg/kg
   Females: LD_{50} > 5000 mg/kg
   Combined: LD_{50} > 5000 mg/kg
2. **The estimated LD_{50} is greater than 5000 mg/kg for males and females.**
3. **Toxicity Category**: IV **Classification**: Acceptable

Procedure (Deviations from 81-2): Due to an oversight, clinical observations were not recorded on day 12 of the study. This deviation had no impact on the integrity of the study.

Results:

Reported Mortality

Dosage (mg/kg)	(Number Deaths/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: All animals were active and healthy through the study. Erythema and edema were observed on all animals at the 24-hour observation on all animals except for one male who had no edema at the 24-hour observation. .At the 14-day observation, one female had no erythema; however, shiny areas, flaking skin, and cracking skin were observed. Three males had no edema and one female had no edema. Two males had few feces.

Gross Necropsy Findings: Gross necropsies were unremarkable.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (81-4, 870.2400)

Product Manager: Velma Noble
MRID No.: 49445604

Reviewer: Chris Jiang
Study Completion Date: Jan. 24, 2014
Study No.: MB 13-22158.04

Testing Laboratory: MB Research Laboratories
Author: Debra A. Hall

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: DS 6421 Express Liquid, lot 5966-076B, clear colorless liquid
Dosage: 0.1 mL

Species: One male and two female New Zealand White rabbits
Age: Thirty-two weeks
Pretest Weight: ♂: 3.3 kilograms; ♀: 3.2 to 3.3 kilograms
Source: Covance Research Products, Inc., Denver, PA

Summary:

1. **Toxicity Category**: II
2. **Classification**: Acceptable

Procedure (Deviations from 81-4): No deviations occurred during the study.

Results:

Individual Scores for Ocular Irritation

Observations	Rabbit No. H6642 (Male)					
	Time After Treatment					
	1 hr	24 hrs	48 hrs	72 hrs	day 7	day 14
I. Corneal Opacity	0	0[1]	0	0	0	0[1]
II. Iritis	0	0	0	0	0	0
III. Conjunctivae						
A. Redness	1	0	0	0	0	0
B. Chemosis	0	0	0	0	0	0
C. Discharge	1	0	0	0	0	0
Observations	**Rabbit No. H6672 (Female)**					
	Time After treatment					
	1 hr	24 hrs	48 hrs	72 hrs	day 7	day 14
I. Corneal Opacity	0	0[1]	0	0	0	0
II. Iritis	0	0	0	0	0	0
III. Conjunctivae						
A. Redness	1	0	0	0	0	0
B. Chemosis	1	0	0	0	0	0
C. Discharge	1	0	0	0	0	0
Observations	**Rabbit No. H6673 (Female)**					
	Time After Treatment					
	1 hr	24 hrs	48 hrs	72 hrs	day 7	day 14
I. Corneal Opacity	0	0[1]	0	0	0[1]	0
II. Iritis	0	1	0	0	0	0
III. Conjunctivae						
A. Redness	1	2	2	2	1	0
B. Chemosis	2	2	2	2	2	0
C. Discharge	2	2	2	2	0	0

Sodium fluorescein was used at the 24-hour observation to verify the absence of corneal opacity

DATA REVIEW FOR PRIMARY SKIN IRRITATION TESTING (81-5, 870.2500)

Product Manager: Velma Noble
MRID No.: 49445604
Reviewer: Chris Jiang
Study Completion Date: Jan. 23, 2014
Study No. MB 13-22158.03
Testing Laboratory: MB Research Laboratories
Author: Blair Yasso

Quality Assurance (40 CFR 160.12): A statement of GLP compliance was included.

Test Material: DS 6421 Express Liquid, lot 5966-076B, clear colorless liquid
Dosage: 0.5 mL

Species: One male and two female New Zealand White rabbits
Age: Thirty-two weeks
Pretest Weight: ♂: 3.0 kilograms; ♀: 3.0 to 3.3 kilograms
Source: Covance Research Products, Inc., Denver, PA

Summary:

1. **Toxicity Category**: I
2. **Classification**: Acceptable

Procedure (Deviations from 81-5): No deviations occurred during the study.

Results:

Animal number	Erythema/edema after unwrap					
	1 hr	24 hrs	48 hrs	72 hrs	7 days	14 days
H6657M	2/0	1/0	1/0	1/0	2r/0	2rf/0
H6667F	2/1	2/0	1/0	1/0	3cfp/1	1fs/1
H6668F	2/0	2/0	2/0	2/0	2c/0	2f/0

r - reclipped
c - cracking skin
f - flaking skin
p - pale areas
s - shiny areas